

Prodrug

From Wikipedia, the free encyclopedia
(Redirected from Prodrugs)

A **prodrug** is a pharmacological substance (drug) which is administered in an inactive (or significantly less active) form. Once administered, the prodrug is metabolised in vivo into the active compound.

Rationale

The rationale behind the use of a prodrug is generally for Absorption, Distribution, Metabolism, and Excretion (ADME) optimization. Prodrugs are usually designed to improve oral bioavailability - poor absorption from the gastrointestinal tract is usually the limiting factor, and is often due to the chemical properties of the drug.

Equally, the use of a prodrug strategy increases the selectivity of the drug for its intended target. An example of this can be seen in many anti-cancer treatments, in which the reduction of adverse effects is always of paramount importance. Drugs used to target hypoxic cancer cells, through the use of redox-activation, utilise the large quantities of reductase enzyme present in the hypoxic cell to convert the drug into its cytotoxic form, essentially activating it. As the prodrug has low cytotoxicity prior to this activation, there is a markedly lower chance of it "attacking" healthy, non-cancerous cells which reduces the side-effects associated with these chemotherapeutic agents

In rational drug design, the knowledge of chemical properties likely to improve absorption and the major metabolic pathways in the body allows the modification of the structure of new chemical entities for improved bioavailability. However, sometimes the use of a prodrug is unintentional, especially in the case of serendipitous drug discoveries, and the drug is only identified as a prodrug after extensive drug metabolism studies.

Prodrugs also occur naturally.